Structured Product Labeling Validation Procedures for Drug Establishment Registration and Drug Listing

Version 2 Revision 201005011423

This document describes computer instructions for automating the validation of Structured Product Labeling (SPL) release 4 files for the drug establishment registration and drug listing process at FDA. Information on electronic submission may be found in guidance entitled *Providing Regulatory Submissions in Electronic Format – Establishment Registration and Drug Listing.* A link to the latest SPL schema and controlled terminology used in SPL and other technical documents may be found on the FDA Data Standards Council web site at: www.fda.gov/oc/datacouncil/spl.html.

1 SPL Header

1.1 General

General procedures

Procedures

1.1.1.1 XML is well formed and valid against the schema

1.1.2 There are no data elements and attributes in addition to those described in this document

1.1.3 There are no spaces in codes

1.1.4 Codes do not have a codeSystemName attribute

1.1.5 Display names are case insensitive

1.1.6 There are no spaces in id extensions

1.1.7 Letters in Globally Unique Identifiers (GUID) are lower case

1.1.8 There are no empty or incomplete elements except, in certain circumstances, code, title, text, and time (an id has a root, a code has a code system).

1.1.9 Characteristics have a class code of “OBS” or no class code at all.

1.1.10 There is no confidentiality code on anything but inactive ingredients and assigned establishments outside establishment registrations.

1.2 XML references

This is the reference to the character set, stylesheet, name space and schema

```
<?xml version="1.0" encoding="UTF-8"?>

<?xml-stylesheet
   href="http://www.accessdata.fda.gov/spl/stylesheet/spl.xsl"
   type="text/xsl"?>

<document xmlns="urn:hl7-org:v3"
   xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
   xsi:schemaLocation="urn:hl7-org:v3
   http://www.accessdata.fda.gov/spl/schema/spl.xsd">
```

Procedures

1.2.1 XML reference is for version 1.0 and encoding “UTF-8”.

1.2.2 There is an xml-stylesheet reference to http://www.accessdata.fda.gov/spl/stylesheet/spl.xsl

1.2.3 The schemaLocation of the urn:hl7-org:v3 namespace is provided as “http://www.accessdata.fda.gov/spl/schema/spl.xsd”

1.2.4 There are no processing instructions other than the xml and xml-stylesheet declarations.

1.2.5 SPL file name is the id root followed by “.xml”

1.2.6 A submission contains only the SPL file whose name ends in ‘.xml’ and associated image files whose names end in '.jpg'.

1.2.7 All image files associated with the SPL document must be actually referenced from that SPL document.

1.3 Document information

This contains information on the type of document and versioning

```
<document>
   <id root="50606941-3e5d-465c-b4e0-0f5a19eb41d4"/>

   <code
      code="51725-0"
      codeSystem="2.16.840.1.113883.6.1"
      displayName="Establishment registration"/>

   <title>Establishment Registration</title>

   <effectiveTime value="20070424"/>

   <setId root="a30accef-f437-4136-808c-9ed4ada5fcf8"/>
```

```
   <versionNumber value="1"/>
```

Procedures

1.3.1 There is an id

1.3.2 id root is a Globally Unique Identifier (GUID).

1.3.3 id does not have an extension.

1.3.4 id does not match any other id in the document.

1.3.5 id is unique across all documents, sections and any other ids

1.3.6 There is a code

1.3.7 Code system is 2.16.840.1.113883.6.1

1.3.8 Code comes from the *Document type* list

1.3.9 Display name matches the code

1.3.10 There are no figures in the title.

1.3.11 There is an effective time with at least the precision of day in the format YYYYMMDD

1.3.12 There is a setId

1.3.13 setId is a GUID

1.3.14 There is a version number

1.3.15 Value of version number is a whole number > 0

1.3.16 Value of version number is greater than the value of any previously submitted version for the same setId

1.4 Labeler and manufacturing information- NDC Labeler Code Request

Use an empty document body:

```
<document>
   <component>
      <nonXMLBody>
         <text/>
```

1.4.1 Document type

```
<document>
      <code  code="51726-8"
         codeSystem="2.16.840.1.113883.6.1"
         displayName="NDC Labeler Code request"/>
```

Procedures

1.4.1.1 Document code is as above

1.4.1.2 There is no title

1.4.1.3 The document body is empty

1.4.1.4 If a document with the same set id has been previously submitted, then it is Labeler Code Request (51726-8).

1.4.2 Labeler information

```
<document>
  <author>
      <time/>
      <assignedEntity>
         <representedOrganization>
            <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
            <id extension=”0001” root=”2.16.840.1.113883.6.69”/>
            <name>Mann's drug Store</name>
            <contactParty>
```

Procedures

1.4.2.1 There is a labeler organization.

1.4.2.2 There are two ids (except for an initial labeler code request, which should be submitted with only one id.)

1.4.2.3 One id has the root 1.3.6.1.4.1.519.1 with a 9-digit extension

1.4.2.4 There is a name.

1.4.2.6 One id has the root 2.16.840.1.113883.6.69 and an extension (except for an initial labeler code request, which should be submitted without this id)

1.4.2.7 There is no id root besides 1.3.6.1.4.1.519.1 and 2.16.840.1.113883.6.69

1.4.2.8 The id with the root 2.16.840.1.113883.6.69 is not associated with any other document of type “NDC Labeler Code request” with a different setId

1.4.2.9 The set id is not associated with any other id with root 2.16.840.1.113883.6.69

1.4.2.10 The id extension with the root 2.16.840.1.113883.6.69 has 4 or 5 digits

1.4.2.11 There is one contact party

1.4.3 Labeler contact party

This rule set applied to all contact parties, not only the Labeler.

```
<contactParty>

   <addr>
      <streetAddressLine>1625 29th street</streetAddressLine>
      <city>Camden</city>
      <state>NJ</state> <postalCode>08101</postalCode>
      <country>USA</country>
   </addr>

   <telecom value="tel:+1-800-555-1213;ext=112"/>
   <telecom value="mailto:Bob.Jones@acme.com"/>

   <contactPerson>
      <name>Bob Jones</name>
   </contactPerson>

</contactParty>
```

Procedures

1.4.3.1 The contactParty has an addr

1.4.3.2 For addresses (addr) the following rules apply:

```
<addr>
   <streetAddressLine>1625 29th street</streetAddressLine>
   <city>Camden</city>
   <state>NJ</state> <postalCode>08101</postalCode>
   <country>USA</country>
</addr>
```

1.4.3.3 An address has street address line, city, and country

1.4.3.4 Country is composed of letters only

1.4.3.5 If the country is “USA”, then the contact party has a state and postal code

1.4.3.6 If the country is “USA”, then the postal code is 5 digits with optionally a dash followed by 4 numbers

1.4.3.7 If the country is **not** in the *postal code validation* list, then there is a postal code

1.4.3.8 There are two or more <telecom> elements

1.4.3.9 One telecom value begins with “tel:” and is a telephone number

1.4.3.10 For telephone numbers, the following general rules apply:

1.4.3.11 telephone numbers are global telephone numbers;

1.4.3.12 telephone numbers contain no letters or spaces;

1.4.3.13 telephone numbers begin with “+”;

1.4.3.14 include hyphens to separate the country code, area codes and subscriber number;

1.4.3.15 have any extensions separated by “;ext=” (see Uniform Resource Identifier (URI) for Telephone Numbers RFC 3966).

1.4.3.16 One telecom value begins with “mailto:” and encodes an email address.

1.4.3.17 an email address is of the simple form <username>@<dns-name>

1.4.3.18 There is one contact person name

1.4.3.19 A labeler code request has no registrant or establishment information

1.5 Labeler and manufacturing information – Establishment registration

1.5.1 Document type

```
<document>
  <code  code="51725-0"
         codeSystem="2.16.840.1.113883.6.1"
         displayName="Establishment registration"/>
```

Procedures

1.5.1.1 Document type is “Establishment registration” (51725-0), “No change notification” (53410-7) or “Out of business notification” (53411-5)

1.5.1.2 The effective time year matches the current year.

1.5.1.3 There is no title

1.5.1.4 The document body is empty

1.5.1.5 For a No change notification (53410-7) or Out of business notification (53411-5) an Establishment Registration (51725-0) with the same set id has been previously submitted.

1.5.1.6 If a document with the same set id has been previously submitted, then it is an Establishment Registration (51725-0) or No change notification (53410-7).

1.5.2 Registrant information

```
<document>
  <author>
     <assignedEntity>
        <representedOrganization>
           <assignedEntity>

  <assignedOrganization>
  <id extension="100000001" root="1.3.6.1.4.1.519.1"/>
  <name>Acme drug company</name>
  <contactParty>
```

Procedures

1.5.2.1 If the document type is “No change notification” or “Out of business notification”, then there is no registrant information.

1.5.2.2 If the document type is “Establishment registration”, then there is registrant information.

1.5.2.3 There is one id

1.5.2.4 id has the root 1.3.6.1.4.1.519.1 with a 9-digit extension

1.5.2.5 There is one name

1.5.2.6 id is not associated with any other set id for document type “Establishment registration”

1.5.2.7 There is one contact party (see the Procedures for contact party above)

1.5.2.8 Establishment registration has no labeler information (no validation rules defined for it.)

1.5.3 Establishment information

```
<document>
  <author>
     <assignedEntity>
        <representedOrganization> <!-- Manufacturer -->
           <assignedEntity>
              <assignedOrganization> <!-- Registrant -->
                 <assignedEntity>

  <assignedOrganization> <!-- Establishment -->

     <id extension="100000001" root="1.3.6.1.4.1.519.1"/>
     <id extension="123456" root=“2.16.840.1.113883.4.82”/>

     <name>Middleton Manufacturing company</name>
```

```
      <addr>
         <streetAddressLine>123 Burl Road</streetAddressLine>
         <city>Dublin</city>
         <country>IRL</country>
      </addr>

      <contactParty>
```

Procedures

1.5.3.1 If the document type is “No change notification” or “Out of business notification”, then there is no establishment information.

1.5.3.2 If the document type is “establishment registration”, then there are one or more establishments.

1.5.3.3 Each establishment

1.5.3.4 has one or two id elements

1.5.3.5 One id has the root 1.3.6.1.4.1.519.1

1.5.3.6 The id with the root 1.3.6.1.4.1.519.1 has a 9-digit extension

1.5.3.7 The id is not associated with another establishment in the same SPL file.

1.5.3.8 The id is not associated with any other set id for document type “Establishment registration”

1.5.3.9 The id with the root 1.3.6.1.4.1.519.1 along with the establishment postal code (if any) and country match the DUNS number, postal code and country in the Dun and Bradstreet database

1.5.3.10 If there is a second id element, then its root is 2.16.840.1.113883.4.82 and the extension is 7 or 10 digits

1.5.3.11 There is one name

1.5.3.12 Each establishment has an address (see the procedures for addr above.)

1.5.3.13 There is one contact party (see the procedures for contact party above)

1.5.3.14 There is no assigned entity other than for US Agent or Import business.

1.5.4 Establishment US agent

```
<document>
  <author>
     <assignedEntity>
        <representedOrganization> <!-- Manufacturer -->
           <assignedEntity>
              <assignedOrganization> <!-- Registrant -->
                 <assignedEntity>

  <assignedOrganization> <!-- Establishment -->
     <addr><country>IRL</country></addr>

     <assignedEntity>
        <assignedOrganization> <!-- Establishment US Agent -->

           <id extension="100000001" root="1.3.6.1.4.1.519.1"/>

           <name>Simmons Reps Company</name>

           <telecom value="tel:+1-800-555-1212"/>
           <telecom value="mailto:contact@USagent.com"/>

        </assignedOrganization>

        <performance>
           <actDefinition>
              <code
                 code="C73330"
                 codeSystem="2.16.840.1.113883.3.26.1.1"
                 displayName="United States agent"/>
```

Procedures

1.5.4.1 If the country for the establishment is not “USA”, then there is one US agent

1.5.4.2 US agent element has code, code system and display name are as above

1.5.4.3 If the country for the establishment is “USA”, then there is no US agent

1.5.4.4 There is one id

1.5.4.5 id has the root 1.3.6.1.4.1.519.1 with a 9-digit extension

1.5.4.6 There is one name

1.5.4.7 There are two or more telecom elements

1.5.4.8 One telecom value begins with “tel:”

1.5.4.9 Rules for telephone numbers are as above.

1.5.4.10 One telecom value begins with “mailto:”

1.5.4.11 Rules for email addresses are as above.

1.5.5 Import business

```
<document>
  <author>
     <assignedEntity>
        <representedOrganization> <!-- Manufacturer -->
           <assignedEntity>
              <assignedOrganization> <!-- Registrant -->
                 <assignedEntity>

  <assignedOrganization> <!-- Establishment -->
     <addr><country>IRL</country></addr>

     <assignedEntity>
        <assignedOrganization> <!-- Establishment US Agent -->
           <id extension="100000005" root="1.3.6.1.4.1.519.1"/>
           <name>Waytogo importers</name>
           <telecom value="tel:+1-800-555-1214"/>
           <telecom value="mailto:contact@waytogo.com"/>
        </assignedOrganization>

        <performance>
           <actDefinition>
              <code  code="C73599"
                     codeSystem="2.16.840.1.113883.3.26.1.1"
                     displayName="import"/>
```

Procedures

1.5.5.1 If the country code for the establishment is not USA, then there may be one or more import businesses.

1.5.5.2 Each business has code, code system and display name are as above.

1.5.5.3 If the country code for the establishment is USA, then there are no import businesses

1.5.5.4 There is one id

1.5.5.5 id has the root 1.3.6.1.4.1.519.1 with a 9-digit extension

1.5.5.6 There is one name for each business

1.5.5.7 There are two or more telecom elements

1.5.5.8 One telecom value begins with “tel:”

1.5.5.9 Rules for telephone numbers are as above.

1.5.5.10 One telecom value begins with “mailto:”

1.5.5.11 Rules for email addresses are as above.

1.5.6 Establishment operation

```
<document>
  <author>
     <assignedEntity>
        <representedOrganization> <!-- Manufacturer -->
           <assignedEntity>
              <assignedOrganization> <!-- Registrant -->
                 <assignedEntity>
                    <assignedOrganization/> <!-- Establishment -->

<performance>
  <actDefinition>
     <code  code="C43360"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="manufacture"/>
```

Procedures

1.5.6.1 There are one or more establishment operation details (performance act definitions).

1.5.6.2 Each performance act definition has one code.

1.5.6.3 Code system is 2.16.840.1.113883.3.26.1.1

1.5.6.4 Display name matches the code

1.5.6.5 The code comes from the business operations list except for C73599 (import) and C73330 (united states agent)

1.6 Labeler and manufacturing information – Drug Listing

1.6.1 Labeler information

```
<document>
  <code  code="..."
         codeSystem="2.16.840.1.113883.6.1"
         displayName="..."/>

<author>

<assignedEntity>
  <representedOrganization>
    <id extension="100000007" root="1.3.6.1.4.1.519.1"/>
    <name>Acme drug company</name>
```

Procedures

1.6.1.1 Document types considered “drug listing” documents are all but “NDC labeler code request”, “establishment registration”, “no change notification”, and “out of business notification”

1.6.1.2 If a document with the same set id has been previously submitted, then it is not a Labeler Code Request (51726-8), Establishment Registration (51725-0), No Change Notification (53410-7), or Out of Business Notification (53411-5).

1.6.1.3 The document body contains two or more sections

1.6.1.4 One section contains the product data elements

Additional content of labeling validation procedures are found in Section 2.3.4.

1.6.1.5 There is one labeler

1.6.1.6 There is one id

1.6.1.7 id has the root 1.3.6.1.4.1.519.1 with a 9-digit extension

1.6.1.8 The setId is not associated with any top level product with a different NDC Labeler Prefix

1.6.1.9 There is one name

1.6.2 Registrant information

```
<document>
   <author>
      <assignedEntity>
         <representedOrganization>

<assignedEntity>
   <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>

   <assignedOrganization>
      <id extension="100000008" root="1.3.6.1.4.1.519.1"/>
      <name>Acme drug company</name>
```

Procedures

1.6.2.1 There is 0 to 1 registrant

1.6.2.2 If there is a confidentiality code, then the code is “B” and the codeSystem is “2.16.840.1.113883.5.25”

1.6.2.3 If there is a registrant, then there is one id.

1.6.2.4 id has the root 1.3.6.1.4.1.519.1 with a 9-digit extension

1.6.2.5 If there is a registrant, then there is one name

1.6.2.6 There is no other element besides id, name and establishments.

1.6.3 Establishment information

```
<document>
  <author>
     <assignedEntity>
        <representedOrganization> <!-- Labeler -->
           <assignedEntity>
              <assignedOrganization> <!-- Registrant -->

<assignedEntity>
  <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>

  <assignedOrganization>  <!-- Establishment -->
     <id extension="1000000019" root="1.3.6.1.4.1.519.1"/>
     <name>Middleton Manufacturing company</name>
  </assignedOrganization>

  <performance>
     <actDefinition>
        <code  code="C43360"
               codeSystem="2.16.840.1.113883.3.26.1.1"
               displayName="manufacture"/>
```

Procedures

1.6.3.1 If the marketing status code for any of the products is **not** *completed*, then there are one or more establishments.

1.6.3.2 If there is a confidentiality code, then the code is “B” and the code system is “2.16.840.1.113883.5.25”

1.6.3.3 Each establishment has one id extension

1.6.3.4 id has the root 1.3.6.1.4.1.519.1 with a 9-digit extension

1.6.3.5 id is not used for other establishments in the file

1.6.3.6 There is one name

1.6.3.7 Establishment (“assignedOrganization”) has no other element besides id and name.

1.6.3.8 There are one or more business operations.

1.6.3.9 Act definition display name matches code

1.6.3.10 The code comes from the business operations list except for C73599 (import) and C73330 (united states agent)

1.6.3.11 Act definition code matches code for an establishment with same id previously submitted in documents of type “establishment registration”

1.6.3.12 If any of the products without a marketing completion date in this listing has no product source, then establishments with operation of API manufacture (C82401) or manufacture (C43360) are included

1.6.4 Business Operation Product

An establishment may specify products associated with each business operation. The following example shows how the business operations are specified for particular products. It is done by replicating the business operation (actDefinition) elements, and connecting each with one product as shown below:

```
<document>
  <author>
    <assignedEntity><representedOrganization>      <!-- Labeler -->
       <assignedEntity><assignedOrganization>      <!-- Registrant -->
          <assignedEntity><assignedOrganization/>  <!-- Establishment -->
            <performance><actDefinition>
              <code code="C43360"
                    codeSystem="2.16.840.1.113883.3.26.1.1"
                    displayName="manufacture"/>

             <product><manufacturedProduct><manufacturedMaterialKind>
               <code code="0123-12345"
                     codeSystem="2.16.840.1.113883.6.69"/>
             </manufacturedMaterialKind></manufacturedProduct></product>
            </actDefinition></performance>

            <performance><actDefinition>
              <code code="C43360"
                    codeSystem="2.16.840.1.113883.3.26.1.1"
                    displayName="manufacture"/>

             <product><manufacturedProduct><manufacturedMaterialKind>
               <code code="0123-12348"
                     codeSystem="2.16.840.1.113883.6.69"/>
```

Procedures

1.6.4.1 There is zero or one operation-product links for each business operation (actDefinition) and those act definition elements are replicated for each products to which that such business operation applies.

1.6.4.2 Each product link has a code referencing a product code in the document.

2 SPL Body

The beginning of the SPL body

```
<document>
  <component>
     <structuredBody>
```

2.1 Product data elements

The beginning of the product data elements is as follows

```
<component>
  <section>
     <id root="e13a985b-f706-a5c8-e8ef-73891eb1c697"/>
     <code  code="48780-1"
            codeSystem="2.16.840.1.113883.6.1"
            displayName="SPL listing data elements section"/>
     <effectiveTime value="20070424"/>
```

Procedures

2.1.1.1 Code, code system and display name are as above

2.1.1.2 Product data element section has an id

2.1.1.3 id root is a GUID and has no extension.

2.1.1.4 There is an effective time with at least the precision of day in the format YYYYMMDD

2.1.1.5 There is one or more product

2.2 Drug Product

```
<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <code code="0001-0001" codeSystem="2.16.840.1.113883.6.69"/>
        <name>Tazmin <suffix>XR</suffix></name>
        <formCode code="C42998"
                  codeSystem="2.16.840.1.113883.3.26.1.1"
                  displayName="tablet"/>
        <asEntityWithGeneric>
          <genericMedicine>
            <name>tazminate hydrochloride</name>
          </genericMedicine>
```

Procedures

2.2.1.1 There is a product code

2.2.1.2 General rules about the product code are:

2.2.1.3 Code system is 2.16.840.1.113883.6.69

2.2.1.4 Code has two segments separated by a hyphen

2.2.1.5 The first segment is numeric.

2.2.1.6 Segments follow the pattern of 4-4, 5-4 or 5-3

2.2.1.7 The second segment is alpha-numeric (letters must be upper-case).

2.2.1.8 First segment matches an NDC Labeler Code associated with the Labeler id.

2.2.1.9 Code has the same labeler segment as the NDC Product Code of all other top-level products in this document.

2.2.1.10 Code has the same length as the NDC Product Code of all other top-level products in this document (i.e., all NDC Product Codes have the same consistent length and hence all NDC Package Codes have the same consistent configuration.)

2.2.1.11 Code has the same length as any other NDC Product Codes of the same labeler (i.e., all NDC Product Codes by the same labeler have the same consistent length and hence all NDC Package Codes have the same consistent configuration.)

2.2.1.12 There is only one product element for each product code, i.e., the same product is not described more than once

2.2.1.13 There is a name

2.2.1.14 Name contains no special symbols (e.g., no “®” or “™” etc) and no “USP” or dosage forms.

2.2.1.15 There is a form code

2.2.1.16 Form code has the code system 2.16.840.1.113883.3.26.1.1

2.2.1.17 If the product has parts, then the form code is C47916

2.2.1.18 Display name matches the code

2.2.1.19 There is a generic medicine name

2.2.1.20 Generic medicine name contains no special symbols (e.g., no “®” or “™” etc) and no “USP” ” or dosage forms.

2.2.1.21 Generic medicine name contains no suffix.

2.2.1.22 If the NDC Product Code was previously submitted, then the product and generic name, source, active ingredient UNII, dosage form, active ingredient strength, product characteristics of size, shape, color and imprint code are the same as in the most recent submission for this NDC code.

2.2.2 Product source

Product source may be specified under a product

```
<subject>
   <manufacturedProduct>
      <manufacturedProduct>
         <asEquivalentEntity>
```

or under parts

```
<part>
   <partProduct>
      <asEquivalentEntity>
```

the detail is as follows:

```
<asEquivalentEntity classCode="EQUIV">
   <code code="C64637" codeSystem="2.16.840.1.113883.3.26.1.1"/>
   <definingMaterialKind>
      <code  code="source NDC Product Code"
             codeSystem="2.16.840.1.113883.6.69"/>
```

Procedures

2.2.2.1 As equivalent entity class code, code and code system are as above

2.2.2.2 If there is a classCode, it is "EQUIV".

2.2.2.3 Defining material kind code matches an NDC Product Code in a SPL file with a different setId

2.2.2.4 NDC Product Code for the source is not the same as the NDC Product Code for the product

2.2.3 Active ingredient

Ingredients may be specified for products

```
<subject>
   <manufacturedProduct>
      <manufacturedProduct>
         <ingredient/>
```

and parts.

```
<part>
   <partProduct>
      <ingredient/>
```

Active ingredients are specified as follows:

```
<ingredient classCode="ACTIR">
   <quantity>
      <numerator value="10" unit="mg"/>
      <denominator value="1" unit="1"/>
   </quantity>
```

```
   <ingredientSubstance>
      <code code="1234567890" codeSystem="2.16.840.1.113883.4.9"/>
      <name>tazminate malate</name>
```

Procedures

2.2.3.1 Class code for active ingredients are ACTIB, ACTIM or ACTIR

2.2.3.2 If the document type is for ‘bulk ingredient’ (53409-9), then there is one and only one active ingredient.

2.2.3.3 If the product has no parts and is not a part, then there are one or more active ingredients.

2.2.3.4 If the product has parts, then the active ingredients are under parts

2.2.3.5 There is a strength with a numerator and denominator

2.2.3.6 Numerator and denominator have a value greater than zero and a unit

2.2.3.7 If the document type is for ‘bulk ingredient’ (53409-9), then numerator and denominator are the same.

2.2.3.8 Unit comes from the *UCUM units of measures* list

2.2.3.9 There is an ingredient code

2.2.3.10 Code system is 2.16.840.1.113883.4.9

2.2.3.11 There is an ingredient name

2.2.3.12 Name matches the code

2.2.4 Active moiety

```
<ingredient classCode="ACTIR">
      <ingredientSubstance>

<activeMoiety>
  <activeMoiety>
      <code code="0987654321" codeSystem="2.16.840.1.113883.4.9"/>
      <name>tazminic acid</name>
```

Procedures

2.2.4.1 There are one or two active moieties

2.2.4.2 There is an active moiety code

2.2.4.3 Code system is 2.16.840.1.113883.4.9

2.2.4.4 There is an active moiety name for each active moiety

2.2.4.5 Active moiety name does not include any of the names in the *Active moiety validation* (counter ion) list except if the word appears by itself optionally followed by “cation” or “anion” or “ion”.

2.2.4.6 Active moiety name matches the code

2.2.5 Reference Ingredient for Strength

```
<ingredient classCode=“ACTIR”>
  <ingredientSubstance>
     <asEquivalentSubstance>
        <definingSubstance>
           <code code="A123455678" codeSystem="2.16.840.1.113883.4.9"/>
           <name>tazemate formate</name>
```

Procedures

2.2.5.1 If the class code is ACTIR, then there is an asEquivalentSubstance element with a defining substance

2.2.5.2 If the class code is not ACTIR, then there is no asEquivalentSubstance element

2.2.5.3 There is a reference ingredient code

2.2.5.4 Code system is 2.16.840.1.113883.4.9

2.2.5.5 There is a name

2.2.5.6 The name matches the code

2.2.6 Inactive ingredient

```
<ingredient classCode="IACT">
  <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>

     <quantity>
     <numerator value="50" unit="mg"/>
     <denominator value="1" unit="1"/>
  </quantity>

  <ingredientSubstance>
     <code code="010202020" codeSystem="2.16.840.1.113883.4.9"/>
     <name>secret dioxide</name>
```

Procedures

2.2.6.1 There are zero to many inactive ingredients.

2.2.6.2 Class code is IACT

2.2.6.3 If the product has parts, then the inactive ingredients are under parts

2.2.6.4 If there is a confidentiality code, then the code is “B” and the codeSystem is “2.16.840.1.113883.5.25”

2.2.6.5 There may be a strength with a numerator and denominator

2.2.6.6 If there is a strength, then numerator and denominator have a value greater than zero and a unit

2.2.6.7 Unit comes from the *UCUM units of measures* list

2.2.6.8 There is an ingredient code

2.2.6.9 Code system is 2.16.840.1.113883.4.9

2.2.6.10 There is an ingredient name

2.2.6.11 Ingredient name matches the code

2.2.6.12 There is no ingredient other than active ingredient (having class code ACTIM, ACTIR, ACTIB), and inactive ingredient (having class code IACT).

2.2.7 Packaging

Packaging may be specified for the product,

```
<manufacturedProduct>
   <manufacturedProduct>
      <asContent/>
```

for parts,

```
<part>
   <partProduct>
      <asContent/>
```

and for packages.

```
<asContent>
   <containerPackagedProduct>
      <asContent/>
```

The format for packaging specification is:

```
<asContent>
   <quantity>
      <numerator value="100" unit="1">
         <translation code="C48542"
                      codeSystem="2.16.840.1.113883.3.26.1.1"
                      displayName="tablet"/>
      </numerator>
      <denominator value="1"/>
   </quantity>
   <containerPackagedProduct>
      <code code="0001-0001-05" codeSystem="2.16.840.1.113883.6.69"/>
      <formCode code="C43169"
                codeSystem="2.16.840.1.113883.3.26.1.1"
                displayName="bottle"/>
```

Procedures

2.2.7.1 Every top-level product has an “as content” element (optional for parts)

2.2.7.2 Quantity includes a numerator and denominator

2.2.7.3 Numerator has a value greater than zero and a unit

2.2.7.4 If the product has parts, then the initial numerator value and unit is “1”

2.2.7.5 Unit of the numerator of the initial package is the same as the units for the denominators of all the strengths

2.2.7.6 Unit of the numerator of an outer package is the same as the unit for the denominator of the quantity of the inner package

2.2.7.7 If the numerator unit is “1” then it has a translation.

2.2.7.8 If the numerator unit is not “1”, then there is no translation

2.2.7.9 Translation code is from the *unit of presentation* list

2.2.7.10 Code system for the translation code is 2.16.840.1.113883.3.26.1.1

2.2.7.11 Translation display name matches the translation code

2.2.7.12 Translation code agrees with the form code of the contained item. For example, if the form code is “blister pack” (C43168) the translation code is also “blister pack” (C61569) and not “blister”.

2.2.7.13 Denominator has value 1 and either no unit or unit “1”

2.2.7.14 There is a form code and display name

2.2.7.15 Code system for form code is 2.16.840.1.113883.3.26.1.1

2.2.7.16 Display name matches form code

2.2.7.17 There is a container packaged product code for outermost package except for parts

2.2.7.18 Container packaged product code is 10 digits (excluding any hyphens).

2.2.7.19 Code system for NDC Package Code is 2.16.840.1.113883.6.69

2.2.7.20 NDC Package Code contains three segments divided by hyphens.

2.2.7.21 The first two segments of the NDC Package Code matches the NDC Product Code

2.2.7.22 Code is not associated with another set id except under parts.

2.2.7.23 If the NDC Package Code has been previously submitted, then the package form code and quantity value and unit are the same as in the most recent submission for this NDC code.

2.2.7.24 If the NDC Package Code is mentioned elsewhere in the document, then the package form code and quantity value and unit are the same.

2.2.8 Parts

Parts may be specified for the product,

```
<manufacturedProduct>
  <manufacturedProduct>
     <part/>
```

and for part products.

```
<part>
  <partProduct>
     <part/>
```

Products with one or more parts

```
<part>
  <quantity>
     <numerator value="1" unit="1"/>
     <denominator value="1"/>
  </quantity>

  <partProduct>
     <code code="0001-0001" codeSystem="2.16.840.1.113883.6.69"/>
     <name>Tazmin <suffix>XR</suffix></name>

     <formCode code="C42916"
               codeSystem="2.16.840.1.113883.3.26.1.1"
               displayName="capsule, extended release"/>
```

```
      <asEntityWithGeneric>
         <genericMedicine>
            <name>tazminate hydrochloride</name>
```

Procedures

2.2.8.1 If the product form code is ‘C47916’ (KIT), then there must be one or more parts

2.2.8.2 If the product has parts, then at least one part has one or more active ingredients.

2.2.8.3 Each part has an overall quantity

2.2.8.4 If there is an “as content” data element in the part, then the numerator unit is the same as the numerator unit for the “as content” data element

2.2.8.5 If there is no “as content” data element in the part, then the numerator unit is 1

2.2.8.6 If there is a code, then the general rules for product code apply.

2.2.8.7 There is a name

2.2.8.8 Name contains no special symbols (e.g., no “®” or “™” etc) and no “USP” or dosage forms.

2.2.8.9 There is a form code and the procedures for product form code apply.

2.2.8.10 There is a generic medicine name

2.2.8.11 Generic name contains no special symbols (e.g., no “®” or “™” etc).

2.2.8.12 If the NDC Product Code of the part was previously submitted, then the product and generic name, active ingredient UNII, dosage form, active ingredient strength, product characteristics of size, shape, color and imprint code are the same as in the most recent submission for this NDC code.

2.2.8.13 If the NDC Product Code is mentioned elsewhere in the document, then the product and generic name, dosage form, UNII and strength of all ingredients are the same.

2.2.8.14 Procedures for source, ingredients, characteristics and packaging are the same as for products without parts

2.2.9 Marketing category

Marketing category, characteristics and DEA schedule are all connected through the <subjectOf> element which may appear on the main product:

```
<subject>
   <manufacturedProduct>
      <manufacturedProduct/>
      <subjectOf/>
```

or on parts:

```
<part>
   <partProduct/>
   <subjectOf/>
```

The marketing category:

```
<subjectOf>
   <approval>
      <id extension="NDA123456" root="2.16.840.1.113883.3.150"/>
      <code  code="C73594"
             codeSystem="2.16.840.1.113883.3.26.1.1"
             displayName="NDA"/>
      <author>
         <territorialAuthority>
            <territory>
               <code code="USA" codeSystem="2.16.840.1.113883.5.28"/>
```

Procedures

2.2.9.1 There is one marketing category for each product and product part

2.2.9.2 Code comes from the *Marketing category* list.

2.2.9.3 Display name matches the code

2.2.9.4 Code system is 2.16.840.1.113883.3.26.1.1

2.2.9.5 If the code is C73583 (ANADA), C73584 (ANDA), C73585 (BLA), C73588 (conditional NADA), C73593 (NADA, C73594 (NDA), C73605 (NDA authorized generic), C75302 (IND), C80438 (Exempt device), C80440 (Humanitarian Device Exemption), C80441 (Premarket Application), or C80442 (Premarket Notification), then the id root is 2.16.840.1.113883.3.150.

2.2.9.6 If the code is C73603 (OTC monograph final) or C73604 (OTC monograph not final), then the id root is 2.16.840.1.113883.3.149

2.2.9.7 If the code is C73583 (ANADA), then the id extension has the prefix “ANADA”

2.2.9.8 If the code is C73584 (ANDA), then the id extension has the prefix “ANDA” followed by 6 digits

2.2.9.9 If the code is C73585 (BLA), then the id extension has the prefix “BLA” followed by 6 digits

2.2.9.10 If the code is C73593 (NADA) or C73588 (Conditional NADA), then the id extension has the prefix “NADA”

2.2.9.11 If the code is C73594 (NDA) or C73605 NDA authorized generic), then the id extension has the prefix “NDA” followed by 6 digits

2.2.9.12 If the code is C75302 (IND), then the id extension has the prefix “IND” followed by 6 digits

2.2.9.13 If the code is C73603 (OTC monograph final) or C73604 (OTC monograph not final), then the id extension must match a code in the *OTC validation* list.

2.2.9.14 If the code is C80438 (Exempt device), then the id extension consists of 3 letters

2.2.9.15 If the code is C80440 (Humanitarian Device Exemption), then the id extension has a prefix “H” followed by 6 digits

2.2.9.16 If the code is C80441 (Premarket Application), then the id extension has a prefix “P” or “BP” followed by 6 digits

2.2.9.17 If the code is C80442 (Premarket Notification), then the id extension has a prefix “K” or “BK” followed by 6 digits.

2.2.9.18 If the code is C80438 (Exempt device), C80440 (Humanitarian Device Exemption), C80441 (Premarket Application), or C80442 (Premarket Notification), then there is at least one part.

2.2.9.19 If the code is not C73583 (ANADA), C73584 (ANDA), C73585 (BLA), C73588 (Conditional NADA), C73593 (NADA), C73594 (NDA), C73603 (OTC monograph final), C73604 (OTC monograph not final), C73605 (NDA authorized generic), C75302 (IND), C80438 (Exempt device), C80440 (Humanitarian Device Exemption), C80441 (Premarket Application) or C80442 (Premarket Notification) then there is no id.

2.2.9.20 If the document type code is: 50577-6 (OTC animal drug), 50576-8 (OTC type A), 50574-3 (OTC type B), 50573-5 (OTC type C), 50578-4 (prescription animal drug), 50575-0 (VFD type A), 50572-7 (VFD type B) or 50571-9 (VFD type C), then the marketing category is: C73583 (ANADA), C73588 (Conditional NADA), C73593 (NADA), C73614 (unapproved homeopathic), C73613 (unapproved medical gas) or C73627 (unapproved drug other).

2.2.9.21 If the marketing category is C73583 (ANADA), C73588 (Conditional NADA), C73593 (NADA), then the document type code is: 50577-6 (OTC animal drug), 50576-8 (OTC type A), 50574-3 (OTC type B), 50573-5 (OTC type C), 50578-4 (prescription animal drug), 50575-0 (VFD type A), 50572-7 (VFD type B) or 50571-9 (VFD type C)

2.2.9.22 If the marketing category is C73626 (bulk ingredient), then the document type is 53409-9 (bulk ingredient).

2.2.9.23 If the document type is 53409-9 (bulk ingredient), then the marketing category is C73626 (bulk ingredient)

2.2.9.24 Territorial authority is as above

2.2.10 Marketing date

```
<subject>
  <manufacturedProduct>

<subjectOf>
  <marketingAct>
     <code code="C53292" codeSystem="2.16.840.1.113883.3.26.1.1"/>
     <statusCode code="active"/>
     <effectiveTime>
        <low value="20040120"/>
```

Procedures

2.2.10.1 There is one marketing status code for each top-level product (part products do not need this)

2.2.10.2 Code is C53292 and code system is 2.16.840.1.113883.3.26.1.1.

2.2.10.3 Status code is *active* or *completed*

2.2.10.4 If the status code is *active*, then there is a low value and no high value

2.2.10.5 If the code is *completed*, then there is a low and high value

2.2.10.6 The effective time low and high boundary have at least the precision of day in the format YYYYMMDD

2.2.10.7 If there is a high value, then it is not less than the low value.

2.2.11 DEA schedule

```
<subjectOf>
  <policy classCode="DEADrugSchedule">

     <code  code="C48675"
        codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="CII"/>
```

Procedures

2.2.11.1 If there is a DEA schedule, then the code system is 2.16.840.1.113883.3.26.1.1

2.2.11.2 Display name matches the code

2.2.11.3 The policy element has a class code of ‘DEADrugSchedule’.

2.2.12 Color

```
<subjectOf>
  <characteristic>
     <code code="SPLCOLOR" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value code="C48333"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="blue" xsi:type="CE">
        <originalText>LIGHT BLUE</originalText>
```

Procedures

2.2.12.1 If the dosage form is on the *solid oral dosage form* list, then there is a color.

2.2.12.2 Code and code system is as above

2.2.12.3 Value code system is 2.16.840.1.113883.3.26.1.1

2.2.12.4 Display name matches the value code

2.2.13 Shape

```
<subjectOf>
  <characteristic>
     <code code="SPLSHAPE" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value code="C48336"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="capsule" xsi:type="CE"/>
        <originalText>capsule like</originalText>
```

Procedures

2.2.13.1 If the dosage form is on the *solid oral dosage form* list, then there is a shape

2.2.13.2 Code and code system is as above

2.2.13.3 Value code system is 2.16.840.1.113883.3.26.1.1

2.2.13.4 Display name matches the value code

2.2.13.5 There is only one shape element

2.2.14 Size

```
<subjectOf>
  <characteristic>
     <code code="SPLSIZE" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value unit="mm" value="18" xsi:type="PQ"/>
```

Procedures

2.2.14.1 If the dosage form is on the *solid oral dosage form* list, then there is a size

2.2.14.2 Code and code system is as above

2.2.14.3 There is a unit and value

2.2.14.4 Value units is mm

2.2.14.5 Value is a whole number greater than zero

2.2.14.6 There is only one size element

2.2.15 Scoring

```
<subjectOf>
  <characteristic>
     <code code="SPLSCORE" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value value="1" xsi:type="INT"/>
```

Procedures

2.2.15.1 If the dosage form is on the *solid oral dosage form* list, then there is scoring

2.2.15.2 Code and code system is as above

2.2.15.3 The value is 1, 2, 3, 4 or nullFlavor=”OTH”

```
  <characteristic>
     <code code="SPLSCORE" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value nullFlavor=“OTH” xsi:type="INT"/>
```

2.2.15.4 There is only one score element

2.2.16 Imprint code

```
<subjectOf>
  <characteristic>
     <code code="SPLIMPRINT" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value xsi:type="ST">05</value>
```

Procedures

2.2.16.1 Code and code system is as above

2.2.16.2 Value has only letters and numbers separated by semicolon without spaces

2.2.16.3 There is only one imprint code element

2.2.17 Flavor

```
<subjectOf>
  <characteristic>
     <code code="SPLFLAVOR" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value code="C73391"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="grape" xsi:type="CE">
        <originalText>wild grape</originalText>
```

Procedures

2.2.17.1 If there is a flavor, then code and code system is as above

2.2.17.2 Value code system is 2.16.840.1.113883.3.26.1.1

2.2.17.3 Display name matches the value code

2.2.18 “Contains” characteristic

```
<subjectOf>
  <characteristic>
     <code code="SPLCONTAINS" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value code="C00000"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="example" xsi:type="CE">
        <originalText>contains peanuts</originalText>
```

Procedures

2.2.18.1 If there is a “contains” characteristic, then code and code system is as above

2.2.18.2 Value code system is 2.16.840.1.113883.3.26.1.1

2.2.18.3 Display name matches the value code

NOTE: The code list for the “contains” characteristic is pending

2.2.19 Image

```
<subjectOf>
  <characteristic>
     <code code="SPLIMAGE" codeSystem="2.16.840.1.113883.1.11.19255"/>
     <value xsi:type="ED" mediaType="image/jpeg">
        <reference value="8837a946-1912-4c1f-8035-e313fdd11ef2.jpg"/>
```

Procedures

2.2.19.1 If there is SPL image, then code and code system are as above

2.2.19.2 Value xsi:type is as above

2.2.19.3 mediaType is “image/jpeg”

2.2.19.4 Reference value is the file name for the image

2.2.19.5 Image file obtained from FDA has the file name assigned by FDA.

2.2.19.6 The image file is submitted together with the SPL file.

2.2.19.7 There are no characteristics other than the ones mentioned above.

2.2.20 Route of administration

Route of administration may be specified for products

```
<subject>
  <manufacturedProduct>
     <consumedIn/>
```

and their parts:

```
<part>
  <consumedIn/>
```

Route of administration is specified as follows:

```
<consumedIn>
  <substanceAdministration>
     <routeCode   code="C38288"
                  codeSystem="2.16.840.1.113883.3.26.1.1"
                  displayName="oral"/>
```

Procedures

2.2.20.1 If the document type is not for ‘bulk ingredient’ (53409-9) and product is not a top-level product whose form code is C47916, then there is one or more “consumed in” substance administration with route code.

2.2.20.2 Route code system is 2.16.840.1.113883.3.26.1.1

2.2.20.3 There is a display name that matches the code

2.2.20.4 If the document type is for ‘bulk ingredient’ (53409-9), then route code is “not applicable” or not present at all.

```
      <routeCode nullFlavor="NA"/>
```

2.2.20.5 The route code cannot be “not applicable” (C48623) for document types other than bulk ingredient (53409-9).

2.3 Content of labeling

2.3.1 Sections

```
<component>
  <section>
     <id root="62abedf9-6bde-4787-beb0-abd214307427"/>
     <code  code="34067-9"
            codeSystem="2.16.840.1.113883.6.1"
            displayName="Indications and Usage"/>
        <title>Indications and Usage</title>
        <text>labeling text</text>
        <effectiveTime value="20070822"/>
        <component/>
```

Procedures

2.3.1.1 Each section has zero to many subsections

2.3.1.2 Each section and subsection has an id root and no extension

2.3.1.3 id root is a GUID

2.3.1.4 id does not match any other id in the document

2.3.1.5 id does not match any other id across all sections, documents, or any id other than the id of the same section previously submitted

2.3.1.6 Each section and subsection has a code

2.3.1.7 Code system is 2.16.840.1.113883.6.1

2.3.1.8 Display name matches the code

2.3.1.9 Each section has an effective time with at least the precision of day in the format YYYYMMDD.

2.3.1.10 There are no figures in the title for a section or subsection.

2.3.1.11 Section for Medication Guide (42231-1) and Patient Package Insert (42230-3) is not a subsection.

2.3.2 Images

```
<component>
  <observationMedia ID="MM1">
     <text>descriptive text</text>
     <value xsi:type="ED" mediaType="image/jpeg">
        <reference value="04056a1a-cadb-48d8-b7c5-17d4cda3924b.jpg"/>
     </value>
```

Procedure

2.3.2.1 There is text

2.3.2.2 Media type is image/jpeg

2.3.2.3 Reference value is the file name for the image

2.3.2.4 Size of image file is less than 1 MB

2.3.2.5 File is a JPEG image and the name has the extension ".jpg"

2.3.2.6 Image components are referenced at least once in the text of any section.

2.3.2.7 Image reference in text has an image "observationMedia" element with a matching ID in the same document.

2.3.3 Highlights

```
<section>

<excerpt>
  <highlight>
     <text>...</text>
```

Procedures

2.3.3.1 There may be excerpts.

2.3.3.2 Excerpts occur only in sections with the following codes: 34066-1 (Boxed Warning), 43683-2 (Recent Major Changes), 34067-9 (Indications and Usage), 34068-7 (Dosage and Administration), 43678-2 (Dosage Forms and Strengths), 34070-3 (Contraindications), 43685-7 (Warnings and Precautions), 34084-4 (Adverse Reactions), 34073-7 (Drug Interactions), 43684-0 (Use in Specific Populations), 49489-8 (Microbiology)

2.3.3.3 If there is an excerpt, then it only has highlight text.

2.3.3.4 An excerpt in the adverse reactions section (34084-4) includes the statement: "to report suspected adverse reactions" and "1-800-FDA-1088" (different telephone number for documents of type 53404-0 – “Vaccine Label”).

2.3.3.5 If there are highlights excerpts, then the title for the SPL file includes the text string (without the quotation marks): “These highlights do not include all the information needed to use” “see full prescribing information for” and “Initial U.S. Approval”

2.3.4 Required Content of Labeling Sections

2.3.4.1 If the document is not a UDI submission, then there is a section with the code 51945-4 (principal display panel) with an image of the carton/container label.

2.3.4.2 If the marketing category code is not C73626 (bulk ingredient) or C73613 (unapproved medical gas), then there is at least one other content of labeling section besides those with the codes 48780-1 and 51945-4.

2.3.4.3 If the approval number is in the medication guide validation list, then there must be such a Medication Guide section (42231-1).